

Oral Science International, November 2008, p.135–140  
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## A Case of Squamous Cell Carcinoma Arising from Branchial Cleft Cyst

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**Abstract:** Carcinoma arising from the remnant of branchial epithelium or branchial cleft cyst is known as branchiogenic carcinoma. It is very rare, and its existence is a matter of controversy. We report a case of cystic carcinoma of the upper neck that fully met Martin's criteria for branchiogenic carcinoma. A 53-year-old male visited Tsurumi University Dental Hospital with a swelling on the left side of the neck. Three tumors were excised from the neck, and histopathology revealed squamous cell carcinoma in a cystic lesion. As metastatic carcinoma of the cervical lymph nodes was suspected, the appropriate clinical tests and imaging were performed to determine the possible presence of a primary tumor. However, no primary carcinoma was found. These findings suggest that this was a case of branchiogenic carcinoma. The patient was treated with radiotherapy and followed up over an 8-year period. No evidence of recurrence was found.

**Key words:** branchial cleft cyst, squamous cell carcinoma, branchiogenic carcinoma

### Introduction

A diagnosis of branchiogenic carcinoma is a matter of some controversy. In a review of the literature on malignant branchioma in 1950, Martin<sup>1</sup> *et al.* suggested that the majority of such cases were actually metastatic squamous cell carcinoma with central cystic degeneration from an unknown primary site. This report describes a case of cystic carcinoma of the neck that met the strict diagnostic criteria for branchiogenic carcinoma advocated by Martin<sup>1</sup>, and discusses a number of problems presented by this case.

### Case Report

A 53-year-old Japanese male was admitted to

Tsurumi University Dental Hospital with a swelling in the left side of the neck. Nine months prior to his first medical examination at the hospital, the patient developed a walnut-sized swelling during routine dental treatment at another clinic. Administration of antibiotics decreased the size of the swelling, but failed to eradicate it completely. A blood test and ultrasound imaging were carried out by an internist, but the cause of the swelling remained unclear. Two weeks prior to visiting Tsurumi University Dental Hospital, the patient caught a cold and the swelling re-enlarged. Clinical examination at our hospital revealed that the swelling was covered with normal skin. It was located just anterior to the left sternocleidomastoid muscle in the jugulodigastric area (Fig. 1). Palpation revealed that it was round and the size of a hen's egg. In texture it was elastic and rubbery, allowing some movement, but firm. No other

Received 11/02/07; revised 06/25/08; accepted 07/11/08.

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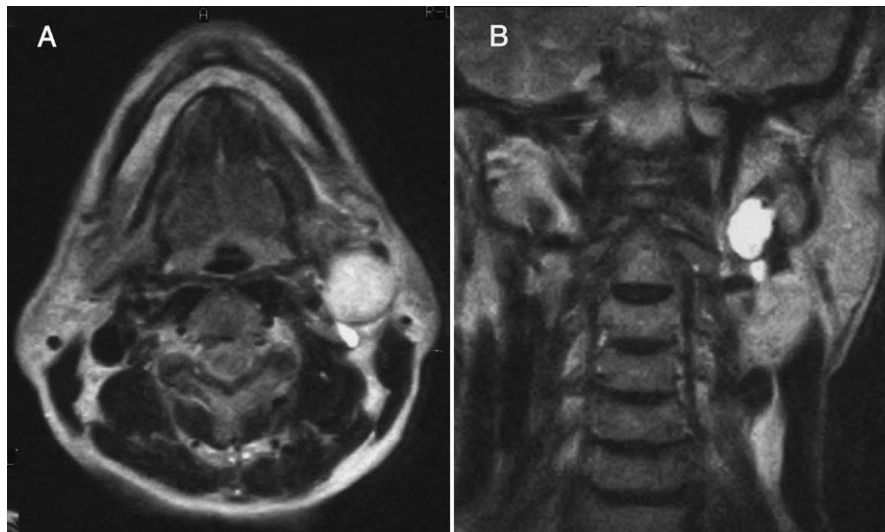
lymphadenopathy was present in the head and neck region. Oral examination and laboratory data revealed no remarkable findings. Magnetic resonance imaging (MRI) revealed a  $30 \times 25 \times 35$  mm, well-demarcated, smooth and round tumor, just below the parotid gland, lateral to the internal jugular vein and posterior to the submandibular gland. Signal intensity was almost equal to that of skeletal muscle on T1-weighted imaging. High signal intensity on T2-weighted imaging indicated the presence of fluid (Fig. 2A). Two other small tumors were observed just superior to



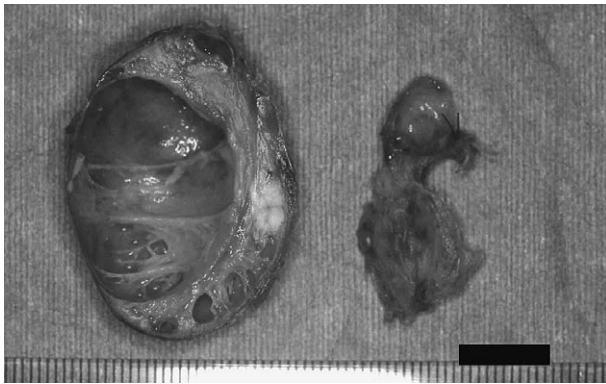
**Fig. 1** Swelling of the neck at first examination.

the main tumor (Fig. 2B). Due to the volume of the tumor, the internal jugular vein was medially deviated. Ultrasound imaging revealed the kind of smooth and round hypoechoic lesion associated with hyperechoic areas. These findings suggested a clinical diagnosis of lateral cervical cyst.

Ten weeks after the first medical examination, surgical excision was performed under general anesthesia. The main tumor was located below the posterior belly of the digastric muscle, anterior to the sternocleidomastoid muscle, and was covered by a fibrous capsule. It was easily dissected from the surrounding tissue. Two small tumors were then identified in the upper area of the surgical field. Resembling lymph nodes in appearance, these were also easily excised. The cut surfaces of the three tumors showed a cystic structure containing yellowish brown fluid. In the largest tumor, the cystic space was divided into several compartments by smooth membranous septi (Fig. 3). The histopathological diagnosis of the three tumors was squamous cell carcinoma. We suspected that they were metastatic carcinoma to the cervical lymph nodes from an unknown primary site. Therefore, the patient was referred to an otorhinolaryngologist for a thorough examination, includ-



**Fig. 2** A: Horizontal T2-weighted magnetic resonance imaging reveals  $30 \times 25 \times 35$  mm cystic lesion containing fluid located below the parotid gland, lateral to the jugular vein and carotid artery, and posterior to the submandibular gland.  
B: T2-weighted imaging reveals two small tumors with high signal intensity just superior to the main tumor.

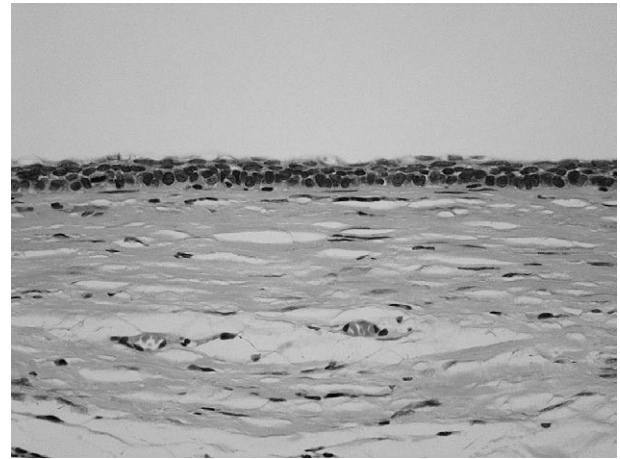


**Fig. 3** Cut surface of the excised three cystic tumors. The two small tumors (right) are connected with each other by fibrous connective tissue. The largest one (left) has a partially thickened cystic wall and smooth membranous septi.

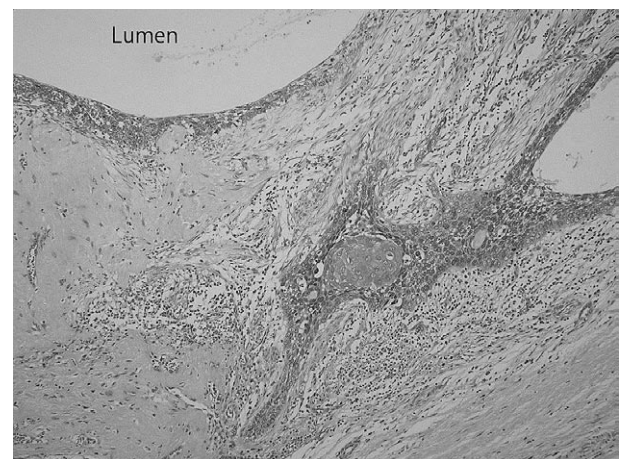


**Fig. 4** Low-power photomicrograph of the largest cystic tumor. Non-tumorous lining epithelium (arrow) evolves to squamous cell carcinoma (black arrowhead) and shows focal invasion to subcapsular connective tissue (open arrowhead). (Hematoxylin and eosin, original magnification  $\times 40$ )

ing computed tomography of the head and neck, endoscopy of the respiratory tract and upper digestive tract, and scintigraphy using gallium and technetium. However, no primary site was detected. Because the operation was not en bloc neck dissection, 45 days after surgery radiotherapy at a total dose of 50 Gy with a 4-MV Linac was applied to the surgical field ( $80 \times 100$  mm) to prevent recurrence. The patient has been free of the disease for 8 years following radiotherapy.



**Fig. 5** High-power photomicrograph of non-tumorous area of the largest cystic tumor. Lining epithelium consists of a cuboidal basal cell layer and one to two layers of flattened squamous cells without epithelial dysplasia. (Hematoxylin and eosin, original magnification  $\times 200$ )

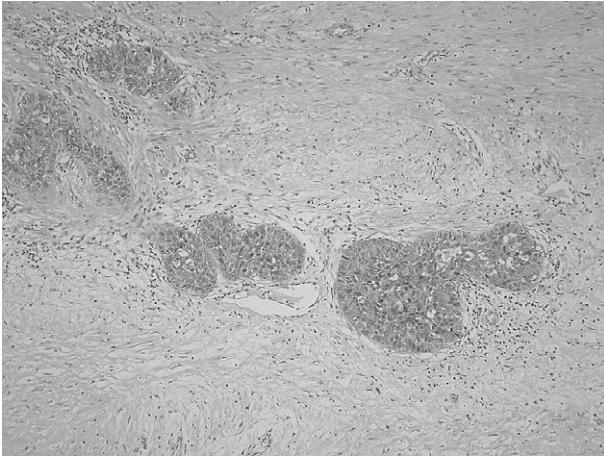


**Fig. 6** Magnified view of the area shown with the black arrowhead in Fig. 4. (Hematoxylin and eosin, original magnification  $\times 100$ )

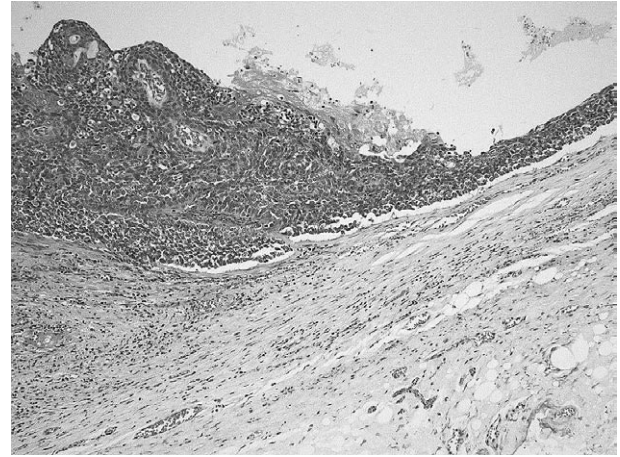
### Histopathological findings

The largest cystic lesion revealed an outer layer consisting of fibrous connective tissue (Fig. 4). The cystic lumen was lined with cuboidal basal cells and one to two layers of flattened squamous epithelium (Fig. 5). Most of these cells showed no atypia or mitotic figures. In some areas, lining epithelium increased the thickness associated with epithelial dysplasia (Figs. 4 and 6). Furthermore, these dysplastic epithelial cells focally showed nodular projections into the cystic lumen and infiltrated into the subepithelial fibrous con-

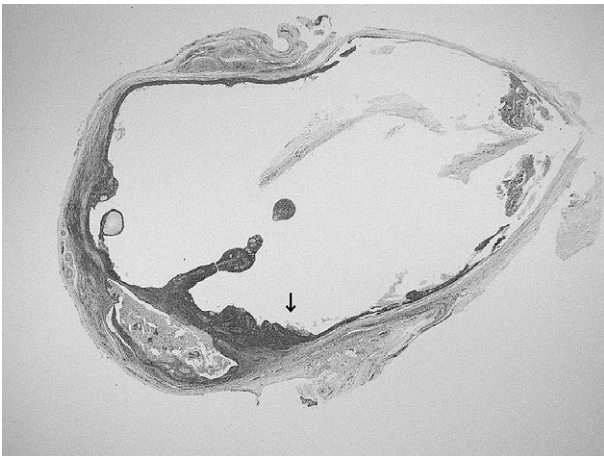




**Fig. 7** Invasive tumor shows squamous differentiation and epithelial cell nests focally infiltrating into subepithelial fibrous connective tissue. (Hematoxylin and eosin, original magnification  $\times 100$ )



**Fig. 9** Magnified view of the area shown with the arrow in Fig. 8. Lining epithelium with epithelial dysplasia (right) evolves to squamous cell carcinoma with keratinization (left). (Hematoxylin and eosin, original magnification  $\times 100$ )



**Fig. 8** Low-power photomicrograph of one of the two small cystic tumors. Lining epithelium shows the same histological findings as the largest cystic tumor. (Hematoxylin and eosin, original magnification  $\times 20$ )

nective tissue with keratinization (Figs. 4 and 6). These invasive cells showed marked cellular atypism, suggesting malignant transformation (Fig. 7). These findings were compatible with squamous cell carcinoma arising from the preexisting cyst. The other two small cystic lesions showed the same basic histopathological findings as this largest one, namely, non-tumorous lining epithelium, epithelial dysplasia and squamous cell carcinoma (Figs. 8 and 9). The final histopathological diagnosis was squamous cell carcinoma of branchiogenic origin.

## Discussion

The first report of a carcinoma arising in a branchial cleft cyst was published by Von Volkmann<sup>2</sup> in 1882. Martin<sup>1</sup> *et al.* proposed the following criteria for the diagnosis of branchiogenic carcinoma:

(1) The cervical tumor must have occurred somewhere along a line extending from a point just anterior to the tragus of the ear, downward along the anterior border of the sternocleidomastoid muscle to the clavicle.

(2) The histological appearance of the growth must be consistent with an origin from tissue known to be present in branchial vestigia.

(3) The patient must have survived and have been followed by periodic examinations for at least five years without the development of any other lesion which could possibly have been the primary tumor.

(4) The best criterion of all would be the histologic demonstration of a cancer developing in the wall of an epithelial-lined cyst situated in the lateral aspect of the neck.

Further to this, Wolff<sup>3</sup> *et al.* added the criterion that the lining epithelium should demonstrate a step-wise escalation from normal, to atypical, to intra-epithelial cancer to frankly invasive cancer. This case met not only Martin's criteria, but also Wolff's additional criterion. However, the possibil-

ity that radiotherapy following surgical excision might have induced a complete response, completely eradicating a previously undetected minute primary carcinoma within the irradiated field in the head and neck region, cannot be ruled out.

A review of 67 branchiogenic carcinoma cases reported in the English-language literature was carried out by Khafif<sup>4</sup> *et al.* According to their report, postoperative radiotherapy successfully controlled an occult primary tumor over a 5-year period in a significant number of patients. Therefore, two new criteria were advocated in place of Martin's third criterion of a 5-year follow-up with no identification of a primary tumor elsewhere. This furnishes us with a strict but reasonable set of criteria for the establishment of a diagnosis of branchiogenic carcinoma. The criteria are as follows:

1. Location of the tumor in the anatomic region of the branchial cleft cyst or sinus as defined by Martin *et al.*

2. Histologic appearance of the tumor consistent with its origin from branchial vestiges; *i.e.*, squamous cell carcinoma.

3. Presence of the carcinoma within the lining of an identifiable epithelial cyst.

4. Identification of transition from the normal squamous epithelium of the cyst to carcinoma.

5. Absence of any identifiable primary malignant tumor after exhaustive evaluation of the patient.

In this case, none of the three tumors showed the type of lymphoid element in the cyst wall that is generally observed in a branchial cyst. Some reports, however, have shown that a branchial cyst does not necessarily have lymphoid tissue<sup>5,6</sup>. Considering the origin of a branchial cleft cyst, a cyst wall that has developed from an endomorphic branchial pouch should contain lymphoid elements. On the other hand, a cyst wall that has developed from an ectomorphic branchial groove would not necessarily contain such lymphoid elements.

A cystic carcinoma with adjacent lymph nodes was reported<sup>7</sup>. However, the occurrence of three cystic tumors in one patient is quite rare. It was speculated that multiple carcinomatous changes

occurred along the course of the branchial tract, or that a branchiogenic carcinoma metastasized to two adjacent lymph nodes. None of the three cystic tumors here, however, contained lymphoid tissue, favoring the former theory.

Including our case, 103 cases of branchiogenic carcinoma have been reported in Japan. In one report, Katori *et al.*<sup>8</sup> summarized 101 cases of branchiogenic carcinoma in Japan. According to their study, the male to female ratio was 2.5:1; average age was 59.1 years old; mortality was 48%, and average survival time was 10.5 months.

A wide resection with radical neck dissection is recommended as the treatment of choice. Postoperative chemotherapy and/or radiotherapy are necessary when invasion to surrounding tissue is evident<sup>8</sup>. We believe that the main reason for the excellent clinical course in this patient was that the carcinoma did not invade the surrounding soft tissue. Additionally, postoperative radiotherapy might be appropriate.

In conclusion, even now, a preoperative diagnosis of branchiogenic carcinoma is difficult<sup>9</sup>. However, this case suggests that in evaluating a swelling of the neck, branchiogenic carcinoma should also be considered as a possible diagnosis, in addition to metastatic carcinoma of an unknown primary site.

#### Acknowledgements

We would like to thank professor Sugisaki for his helpful suggestions.

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